AMENDMENTS TO THE CLAIMS

Please add claims 154-160 as indicated below. This listing of claims will replace all prior versions, and listings, of claims in the application:

5 Listing of Claims:

1-37. (canceled)

38. (previously presented) The compound according to claims 62 or 68, selected from the group consisting of:

10

223b

307b

820b

823b H₃C N H OH CI ;

823e

826e OH CI

5

1029 $H_2N \longrightarrow 0$ $N \longrightarrow 0$

39. (previously presented) The compound according to claim 62, selected from the group consisting of:

605j

605m

605n

6050 ;

605p

605q OH H OH H OH

605s OH ;

H₃C N H O H O H

628 H₃C-V OH OH H

5

634 $H_3C \longrightarrow CH$; and $H_1 \longrightarrow H$

635 H₃C O O CH

40. (previously presented) The compound according to claims 62 or 68, selected from the group consisting of:

287 H₃CO H O CI

404 H₃C N OH H

405 $0 \times 10^{10} \times 10^{10$

406 CI.ON NO OH HOOH

407 ON NO OH OH

413 $\begin{array}{c} O \\ O \\ N \\ O \\ O \\ H \end{array} \begin{array}{c} O \\ O \\ N \\ O \\ H \end{array} \begin{array}{c} O \\ O \\ O \\ H \end{array}$

416 $\begin{array}{c} O \\ O \\ N \\ O \\ H \end{array} \begin{array}{c} O \\ O \\ O \\ H \end{array} \begin{array}{c} O \\ O \\ O \\ O \end{array}$

417 ON NO OH OH OH

418 HN H CO N OH H

420 $\begin{array}{c} O \\ N \\ H \end{array} \begin{array}{c} N \\ H \end{array} \begin{array}{c} O \\ \\$

422 N N O N OH H

423

SHOWN OH H

424

N N N OH H

425 HO N CH H

426 $\begin{array}{c} O \\ O \\ N \\ N \\ O \\ H \end{array} \begin{array}{c} O \\ O \\ N \\ H \\ O \end{array}$

430 NH O NH O OH H

431 H_2N H_2N H_2 H_3 H_4 H_5 H_5 H_6 H_7 H_7

435 ,

436 , N O H OH H

43'7

438

439

442

443

444 CI ON NO OH H

457 OH OH

> 459 CI N O CH H O H O

462 F N O N OH H

467 OH HOH

469 H₃C O H O H O H

470 , N O CH CH3

475 OH HO

H₃C O N O OH H

477 HONN OH H

479
HO HO HO HO

481 CL HOH H

482s

483 OH HONN OH H

H₃C N H O H O H O

486

H₃C O H O H O H O

488 H₃C N N O CH

494 ON NO HOH

495 CH

817d

817e , OH O CI

880 OH N-N, N

881 , OH BF4 CI

882

H₃CO H OCI

H₃CO N O CH₃

1006

CI O N O OH H

1007

1008 OH HOH ;

1017
$$CH_3O \longrightarrow H O \longrightarrow H O$$

Page 54 of 135

1041

$$H_3C$$
 CH_3
 C

1052 O N N O H O O H O H O H

> 1053 O N N O N O H

> 1054

1056

N
N
OH
H
OH
H

1058 F H OH H

1061 F O N O OH H

1064 CI N N N N N H OH H

1065 CI N N N N OH H

1079

ON NOTE OF THE OFFICE OF THE OFFICE OF THE OFFICE OF THE OFFICE OFFI

1082
$$\begin{array}{c} CI \\ H_2N \end{array} \begin{array}{c} O \\ H \end{array} \begin{array}{c} O \\ N \\ H \end{array} \begin{array}{c} O \\ N \\ H \end{array} \begin{array}{c} O \\ N \\ H \end{array} \begin{array}{c} O \\ H \\ O \end{array}$$

1093
$$\begin{array}{c} & & & & \\ & & \\ & & & \\ & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & &$$

1095 OH H OOH H

1027
$$\begin{array}{c|c} & & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ \end{array}$$
 and
$$\begin{array}{c|c} & & & \\ & & \\ & & \\ \end{array}$$
 and

41. (canceled)

5

42. (previously presented) A pharmaceutical composition comprising a compound according to any one

of claims 38-40, 57, 62, 66, 68, 79-83, 88-93, 95, 96, 98, 99, 100, 102, 104, 112, 114, 118-131, 133-135 and a pharmaceutically acceptable carrier.

41-54. (canceled)

(previously presented) A method for 5 treating or preventing a disease selected from the group consisting of an IL-1 mediated disease, an apoptosis mediated disease, an inflammatory disease, an autoimmune disease, a destructive bone disorder, a proliferative disorder, an infectious disease, a 10 degenerative disease, a necrotic disease, osteoarthritis, pancreatitis, asthma, adult respiratory distress syndrome, glomeralonephritis, rheumatoid arthritis, systemic lupus erythematosus, scleroderma, chronic thyroiditis, Grave's disease, autoimmune 15 gastritis, insulin-dependent diabetes mellitus (Type I), autoimmune hemolytic anemia, autoimmune neutropenia, thrombocytopenia, chronic active hepatitis, myasthenia gravis, inflammatory bowel disease, Crohn's disease, psoriasis, graft vs host 20 disease, osteoporosis, multiple myeloma-related bone disorder, acute myelogenous leukemia, chronic myelogenous leukemia, metastatic melanoma, Kaposi's

sarcoma, multiple myeloma, sepsis, septic shock,
Shigellosis, Alzheimer's disease, Parkinson's disease,
cerebral ischemia, myocardial ischemia, spinal muscular
atrophy, multiple sclerosis, AIDS-related encephalitis,
HIV-related encephalitis, aging, alopecia, and
neurological damage due to stroke in a patient
comprising the step of administering to said patient a
pharmaceutical composition according to claim 42.

- 56. (previously presented) The method

 according to claim 55, wherein the disease is selected

 from the group consisting of osteoarthritis, acute

 pancreatitis, rheumatoid arthritis, inflammatory bowel

 disease, Crohn's disease, psoriasis, and Alzeheimer's

 disease.
- 57. (previously presented) A compound represented by the formula:

20 wherein:

5

 ${\bf R}_{\bf 1}$ is selected from the group consisting of the following formulae:

(e10)
$$\begin{array}{c} Y_2 \\ R_{21} - X_5 \\ R_5 - N \end{array}$$
;

(e11)
$$R_5-N + O_0$$
;

5 (e12)
$$R_{21}$$
 N N N

(w2)
$$R_8 \longrightarrow 0 \qquad ;$$

$$R_5 \longrightarrow N \longrightarrow C \longrightarrow 0 \qquad ;$$

$$(y2) \qquad \qquad X_7 \xrightarrow{Y_2} \qquad \qquad ;$$

$$(z) \begin{array}{c} Y_2 \\ X_7 \\ N \\ N \end{array} \hspace{1cm} \text{; and}$$

ring C is chosen from the group consisting of benzo, pyrido, thieno, pyrrolo, furano, thiazolo, isothiazolo, oxazolo, isoxazolo, pyrimido, imidazolo, cyclopentyl, and cyclohexyl;

 R_2 is:

5

(a)
$$(r)m$$
 , or OR_{51}

m is 1 or 2;

each $\ensuremath{\text{R}}_5$ is independently selected from the group consisting of:

$$-C(O) - R_{10},$$

$$-C(O) O - R_{9},$$

$$-C(O) - N(R_{10}) (R_{10})$$

$$-S(O)_2 - R_{9},$$

$$-S(O)_2 - NH - R_{10},$$

$$-C(O) - CH_2 - O - R_{9},$$

```
Application No. 10/058,522
        Supp. Amdt. dated March 4, 2004
                      -C(O)C(O)-R<sub>10</sub>
                      -R<sub>9.</sub>
                      -H,
                      -C(0)C(0)-OR_{10} and
                      -C(0)C(0)-N(R_9)(R_{10});
 5
               X_5 is CH or N;
               Y_2 is H_2 or O;
               X_7 is -N(R_8) - or -O-;
10
               R_6 is selected from the group consisting of -H and
         -CH<sub>3</sub>;
               \ensuremath{\text{R}_8} is selected from the group consisting of:
                      -C(0)-R_{10},
15
                      -C(O)O-R9,
                      -C(O)-N(H)-R_{10},
                      -S(0)_2-R_9,
                      -S(O)_{2}-NH-R_{10},
                      -C(0) - CH_2 - OR_{10},
20
                      -C(O)C(O)-R<sub>10</sub>;
                      -C(0) - CH_2N(R_{10})(R_{10}),
                      -C(0) - CH_2C(0) - O - R_9,
                      -C(0) - CH_2C(0) - R_9,
                      -H, and
25
                      -C(0)-C(0)-OR_{10};
```

each R_9 is independently selected from the group consisting of $-Ar_3$ and a $-C_{1-6}$ straight or branched alkyl group optionally substituted with $-Ar_3$, wherein the $-C_{1-6}$ alkyl group is optionally unsaturated;

30

5

10

15

20

25

each R_{10} is independently selected from the group consisting of -H, -Ar₃, a -C₃₋₆ cycloalkyl group, and a -C₁₋₆ straight or branched alkyl group optionally substituted with -Ar₃, wherein the -C₁₋₆ alkyl group is optionally unsaturated;

 R_{13} is selected from the group consisting of H, Ar_3 , and a $-C_{1-6}$ straight or branched alkyl group optionally substituted with $-Ar_3$, $-CONH_2$, $-OR_5$, -OH, $-OR_9$, or $-CO_2H$;

each R_{51} is independently selected from the group consisting of R_9 , $-C(O)-R_9$, $-C(O)-N(H)-R_9$, or each R_{51} taken together forms a saturated 4-8 member carbocyclic ring or heterocyclic ring containing -O-, -S-, or -NH-;

each R_{21} is independently selected from the group consisting of -H or a $-C_{1-6}$ straight or branched alkyl group;

each Ar_3 is a cyclic group independently selected from the set consisting of an aryl group which contains 6, 10, 12, or 14 carbon atoms and between 1 and 3 rings and an aromatic heterocycle group containing between 5 and 15 ring atoms and between 1 and 3 rings, said heterocyclic group containing at least one heteroatom group selected from -O-, -S-, -SO-, SO_2 , =N-, and -NH-, said heterocycle group optionally containing one or more double bonds, said heterocycle group optionally comprising one or more aromatic rings, and said cyclic group optionally being singly or multiply substituted by -Q₁;

each Q_1 is independently selected from the group consisting of -NH $_2$, -CO $_2$ H, -Cl, -F, -Br, -I, -NO $_2$, -CN, =O, -OH, -perfluoro C $_{1-3}$ alkyl, R $_5$, -OR $_5$, -NHR $_5$, -OR $_9$, -N(R $_9$)(R $_{10}$), -R $_9$, -C(O)-R $_{10}$, and

5

CH₂,

provided that when $-Ar_3$ is substituted with a Q_1 group which comprises one or more additional $-Ar_3$ groups, said additional $-Ar_3$ groups are not substituted with another $-Ar_3$.

58-61. (canceled)

15

62. (previously presented) A compound represented by the formula:

(IV)
$$\begin{array}{c} O \\ (\text{IV}) \\ R_1 - N \\ H \end{array}$$

wherein:

m is 1 or 2;

20

 ${\bf R}_{\bf 1}$ is selected from the group consisting of the following formulae:

$$(e10-A)$$

(e11)
$$R_5-N \qquad \qquad ;$$

(e12)
$$R_{21} \longrightarrow N$$

$$(y1) \qquad \begin{array}{c} R_8 \\ N \\ N \\ N \\ N \\ O \\ \end{array} ;$$

$$(y2) \qquad \qquad \begin{matrix} x_7 \\ x_7 \\ y_7 \\$$

10 (z) X_7 X_7 X

ring C is chosen from the group consisting of benzo, pyrido, thieno, pyrrolo, furano, thiazolo,

Supp. Amdt. dated March 4, 2004 isothiazolo, oxazolo, isoxazolo, pyrimido, imidazolo, cyclopentyl, and cyclohexyl; R_3 is selected from the group consisting of: -CN, -C(O)-H, 5 $-C(0) - CH_2 - T_1 - R_{11}$, $-C(0)-CH_2-F$, $-C=N-O-R_9$, and -CO-Ar₂; each R₅ is independently selected from the group 10 consisting of: $-C(0)-R_{10}$, -C(O)O-R9, $-C(0)-N(R_{10})(R_{10})$ $-S(0)_2-R_9$, 15 $-S(0)_2-NH-R_{10}$, $-C(0) - CH_2 - O - R_9$, -C(O)C(O)-R₁₀. -R₉ 20 -H, $-C(O)C(O)-OR_{10}$, and $-C(0)C(0)-N(R_9)(R_{10});$ Y_2 is H_2 or O; X_7 is $-N(R_8)$ - or -O-; 25 each T_1 is independently selected from the group

Application No. 10/058,522

 $\ensuremath{\text{R}}_6$ is selected from the group consisting of -H and

consisting of. -O-, -S-, -S(0)-, and -S(0) $_2$ -;

```
Application No. 10/058,522
        Supp. Amdt. dated March 4, 2004
        -CH3;
               R<sub>8</sub> is selected from the group consisting of:
                     -C(0)-R_{10},
                     -C(O)O-R9,
                     -C(O)-NH-R_{10},
 5
                     -S(0)_2-R_9,
                     -S(O)_2-NH-R_{10},
                     -C(0) - CH_2 - OR_{10},
                     -C(0)C(0)-R_{10}
                     -C(0) - CH_2 - N(R_{10})(R_{10})
10
                     -C(O) - CH_2C(O) - O - R_9,
                     -C(O) - CH_2C(O) - R_9,
                     -H, and
                     -C(0)-C(0)-OR_{10};
```

each R_9 is independently selected from the group consisting of $-Ar_3$ and a $-C_{1-6}$ straight or branched alkyl group optionally substituted with $-Ar_3$, wherein the $-C_{1-6}$ alkyl group is optionally unsaturated;

each R_{10} is independently selected from the group consisting of -H, -Ar₃, a -C₃₋₆ cycloalkyl group, and a -C₁₋₆ straight or branched alkyl group optionally substituted with -Ar₃, wherein the -C₁₋₆ alkyl group is optionally unsaturated;

each R_{11} is independently selected from the group consisting of:

```
-Ar<sub>4</sub>,

-(CH<sub>2</sub>)<sub>1-3</sub>-Ar<sub>4</sub>,

-H, and

-C(O)-Ar<sub>4</sub>;
```

20

5

10

15

20

25

 R_{15} is selected from the group consisting of -OH, -OAr₃, -N(H)-OH, and -OC₁₋₆, wherein C_{1-6} is a straight or branched alkyl group optionally substituted with -Ar₃, -CONH₂, -OR₅, -OH, -OR₉, or -CO₂H;

each R_{21} is independently selected from the group consisting of -H or a $-C_{1-6}$ straight or branched alkyl group;

Ar₂ is independently selected from the following group, in which any ring may optionally be singly or multiply substituted by $-Q_1$ or phenyl, optionally substituted by Q_1 :

$$(hh)$$
 , and

wherein each Y is independently selected from the group consisting of O and S;

each Ar_3 is a cyclic group independently selected from the set consisting of an aryl group which contains 6, 10, 12, or 14 carbon atoms and between 1 and 3 rings and an aromatic heterocycle group containing between 5 and 15 ring atoms and between 1 and 3 rings, said heterocyclic group containing at least one heteroatom group selected from -O-, -S-, -SO-, SO_2 , =N-, and -NH-, $-N(R_5)$ -, and $-N(R_9)$ - said heterocycle group optionally containing one or more double bonds, said heterocycle group optionally comprising one or more aromatic rings,

5

10

15

20

25

30

and said cyclic group optionally being singly or multiply substituted by $-Q_1$;

each Ar_4 is a cyclic group independently selected from the set consisting of an aryl group which contains 6, 10, 12, or 14 carbon atoms and between 1 and 3 rings, and a heterocycle group containing between 5 and 15 ring atoms and between 1 and 3 rings, said heterocyclic group containing at least one heteroatom group selected from -O-, -S-, -SO-, SO_2 , =N-, -NH-, -N(R_5)-, and -N(R_9)- said heterocycle group optionally containing one or more double bonds, said heterocycle group optionally comprising one or more aromatic rings, and said cyclic group optionally being singly or multiply substituted by -Q₁;

each Q_1 is independently selected from the group consisting of $-NH_2$, $-CO_2H$, -Cl, -F, -Br, -I, $-NO_2$, -CN, =O, -OH, -perfluoro C_{1-3} alkyl, R_5 , $-OR_5$, $-NHR_5$, $-OR_9$, $-N(R_9)$ (R_{10}) , $-R_9$, -C(O) $-R_{10}$, and O CH_2 ;

provided that when $-\mathrm{Ar}_3$ is substituted with a Q_1 group which comprises one or more additional $-\mathrm{Ar}_3$ groups, said additional $-\mathrm{Ar}_3$ groups are not substituted with another $-\mathrm{Ar}_3$.

63-65. (canceled)

66. (previously presented) A compound represented by the formula:

$$(V) \qquad \qquad (\bigcap_{m} R_{5}$$

wherein:

5

10

m is 1 or 2;

 R_1 is:

(e10-B)

 ${\bf R_3}$ is selected from the group consisting of:

-CN,

-C(O)-H,

 $-C(O)-CH_2-T_1-R_{11}$,

 $-C(0)-CH_2-F$,

 $-C=N-O-R_9$, and

-CO-Ar2;

each R_5 is $-C(0)C(0)-OR_{10}$;

 Y_2 is H_2 or O;

each T_1 is independently selected from the group consisting of -O-, -S-, -S(O)-, and -S(O)₂-;

each R_9 is independently selected from the group consisting of $-Ar_3$ and a $-C_{1-6}$ straight or branched alkyl group optionally substituted with $-Ar_3$, wherein the $-C_{1-6}$ alkyl group is optionally unsaturated;

each R_{10} is independently selected from the group consisting of -H, -Ar₃, a -C₃₋₆ cycloalkyl group, and a -C₁₋₆ straight or branched alkyl group optionally substituted with -Ar₃, wherein the -C₁₋₆ alkyl group is optionally unsaturated;

each R_{11} is independently selected from the group consisting of:

- $-Ar_4$,
- $-(CH_2)_{1-3}-Ar_4$,
- -H, and

10

15

20

 $-C(0) -Ar_4;$

 $\rm R_{15}$ is selected from the group consisting of -OH, -OAr_3, -N(H)-OH, and -OC_{1-6}, wherein C_{1-6} is a straight or branched alkyl group optionally substituted with -Ar_3, -CONH_2, -OR_5, -OH, -OR_9, or -CO_2H;

each R_{21} is independently selected from the group consisting of -H or a $-C_{1-6}$ straight or branched alkyl group;

Ar₂ is independently selected from the following group, in which any ring may optionally be singly or multiply substituted by $-Q_1$ or phenyl, optionally substituted by Q_1 :

$$(hh)$$
 , and

5

10

15

20

25

wherein each Y is independently selected from the group consisting of O and S;

each Ar_3 is a cyclic group independently selected from the set consisting of an aryl group which contains 6, 10, 12, or 14 carbon atoms and between 1 and 3 rings and an aromatic heterocycle group containing between 5 and 15 ring atoms and between 1 and 3 rings, said heterocyclic group containing at least one heteroatom group selected from -O-, -S-, -SO-, SO_2 , =N-, and -NH-, -N(R_5)-, and -N(R_9)- said heterocycle group optionally containing one or more double bonds, said heterocycle group optionally comprising one or more aromatic rings, and said cyclic group optionally being singly or multiply substituted by -Q1;

each Ar_4 is a cyclic group independently selected from the set consisting of an aryl group which contains 6, 10, 12, or 14 carbon atoms and between 1 and 3 rings, and a heterocycle group containing between 5 and 15 ring atoms and between 1 and 3 rings, said heterocyclic group containing at least one heteroatom group selected from -O-, -S-, -SO-, SO_2 , =N-, -NH-, -N(R_5)-, and -N(R_9)- said heterocycle group optionally containing one or more double bonds, said heterocycle group optionally comprising one or more aromatic rings, and said cyclic group optionally being singly or multiply substituted by -Q1;

each Q_1 is independently selected from the group

consisting of -NH₂, -CO₂H, -Cl, -F, -Br, -I, -NO₂, -CN, =O, -OH, -perfluoro C_{1-3} alkyl, R_5 , -OR₅, -NHR₅, -OR₉, -N(R₉)(R₁₀), -R₉, -C(O)-R₁₀, and O/

5

10

CH₂;

provided that when -Ar $_3$ is substituted with a Q $_1$ group which comprises one or more additional -Ar $_3$ groups, said additional -Ar $_3$ groups are not substituted with another -Ar $_3$.

67. (canceled)

68. (previously presented) A compound represented by the formula:

15

$$(N)$$
 R_1
 R_3
 R_4

wherein:

m is 1 or 2;

R₁ is:

20

 $\ensuremath{\mathtt{R}}_3$ is selected from the group consisting of: -CN,

```
Application No. 10/058,522

Supp. Amdt. dated March 4, 2004

-C(O)-H,

-C(O)-CH<sub>2</sub>-T<sub>1</sub>-R<sub>11</sub>,

-C(O)-CH<sub>2</sub>-F,

-C=N-O-R<sub>9</sub>, and

-CO-Ar<sub>2</sub>;
```

each R_5 is independently selected from the group consisting of:

```
-C(O) - R_{10},
-C(O) O - R_{9},
-C(O) - N(R_{10}) (R_{10})
-S(O)_2 - R_9,
-S(O)_2 - NH - R_{10},
-C(O) - CH_2 - O - R_9,
-C(O) C(O) - R_{10},
-R_9,
-H,
-C(O) C(O) - OR_{10}, and
-C(O) C(O) - N(R_9) (R_{10});
20 \qquad Y_2 \text{ is } H_2 \text{ or } O;
```

25

30

each T_1 is independently selected from the group consisting of -O-, -S-, -S(O)-, and -S(O)₂-;

each R_9 is independently selected from the group consisting of $-Ar_3$ and a $-C_{1-6}$ straight or branched alkyl group optionally substituted with $-Ar_3$, wherein the $-C_{1-6}$ alkyl group is optionally unsaturated;

each R_{10} is independently selected from the group consisting of -H, -Ar₃, a -C₃₋₆ cycloalkyl group, and a -C₁₋₆ straight or branched alkyl group optionally

substituted with $-Ar_3$, wherein the $-C_{1-6}$ alkyl group is optionally unsaturated;

each \mathbf{R}_{11} is independently selected from the group consisting of:

-Ar₄,

5

10

15

20

 $-(CH_2)_{1-3}-Ar_4$,

-H, and

 $-C(0) -Ar_4;$

 R_{15} is selected from the group consisting of -OH, -OAr₃, -N(H)-OH, and -OC₁₋₆, wherein C₁₋₆ is a straight or branched alkyl group optionally substituted with -Ar₃, -CONH₂, -OR₅, -OH, -OR₉, or -CO₂H;

each R_{21} is independently selected from the group consisting of -H or a $-C_{1-6}$ straight or branched alkyl group;

Ar₂ is independently selected from the following group, in which any ring may optionally be singly or multiply substituted by $-Q_1$ or phenyl, optionally substituted by Q_1 :

$$(hh)$$
 , and

wherein each Y is independently selected from the group consisting of O and S;

5

10

15

20

25

30

each Ar_3 is a cyclic group independently selected from the set consisting of an aryl group which contains 6, 10, 12, or 14 carbon atoms and between 1 and 3 rings and an aromatic heterocycle group containing between 5 and 15 ring atoms and between 1 and 3 rings, said heterocyclic group containing at least one heteroatom group selected from -O-, -S-, -SO-, SO_2 , =N-, and -NH-, $-N(R_5)$ -, and $-N(R_9)$ - said heterocycle group optionally containing one or more double bonds, said heterocycle group optionally comprising one or more aromatic rings, and said cyclic group optionally being singly or multiply substituted by $-Q_1$;

each Ar_4 is a cyclic group independently selected from the set consisting of an aryl group which contains 6, 10, 12, or 14 carbon atoms and between 1 and 3 rings, and a heterocycle group containing between 5 and 15 ring atoms and between 1 and 3 rings, said heterocyclic group containing at least one heteroatom group selected from -O-, -S-, -SO-, SO_2 , =N-, -NH-, $-N(R_5)$ -, and $-N(R_9)$ - said heterocycle group optionally containing one or more double bonds, said heterocycle group optionally comprising one or more aromatic rings, and said cyclic group optionally being singly or multiply substituted by $-Q_1$;

each Q_1 is independently selected from the group consisting of $-NH_2$, $-CO_2H$, -Cl, -F, -Br, -I, $-NO_2$, -CN, =0, -OH, -perfluoro C_{1-3} alkyl, R_5 , $-OR_5$, $-NHR_5$, $-OR_9$, $-N(R_9)$ (R_{10}) , $-R_9$, -C(O) $-R_{10}$, and O / CH_2 ;

provided that when $-Ar_3$ is substituted with a Q_1 group which comprises one or more additional $-Ar_3$ groups, said additional $-Ar_3$ groups are not substituted with another $-Ar_3$;

provided that when:

m is 1; R₁₅ is -OH; R₂₁ is -H; and

5

10

15

25

 Y_2 is O and R_3 is -C(O)-H, then R_5 cannot be:

-C(O)- R_{10} , wherein R_{10} is -Ar $_3$ and the Ar $_3$ cyclic group is phenyl, unsubstituted by -Q $_1$, 4- (carboxymethoxy)phenyl, 2-fluorophenyl, 2-pyridyl, N- (4-methylpiperazino)methylphenyl, or

-C(O)-OR $_9$, wherein R $_9$ is -CH $_2$ -Ar $_3$, and the Ar $_3$ cyclic group is phenyl, unsubstituted by -Q $_1$; and when

 Y_2 is O, R_3 is $-C(O)-CH_2-T_1-R_{11}$, T_1 is O, and R_{11} is Ar_4 , wherein the Ar_4 cyclic group is $5-(1-(4-chlorophenyl)-3-trifluoromethyl)pyrazolyl), then <math>R_5$ cannot be:

20 -H;

-C(O)- R_{10} , wherein R_{10} is -Ar $_3$ and the Ar $_3$ cyclic group is 4-(dimethylaminomethyl)phenyl, phenyl, 4-(carboxymethylthio)phenyl,4-(carboxyethylthio)phenyl, 4-(carboxyethyl)phenyl, 4-(carboxyethyl)phenyl, 2-fluorophenyl, 2-pyridyl, N-(4-methylpiperazino)methylphenyl, or

 $-C(O)-OR_9$, wherein R_9 is isobutyl or $-CH_2-Ar_3$ and the Ar_3 cyclic group is phenyl;

and when R_{11} is Ar_4 , wherein the Ar_4 cyclic group

5

10

15

is 5-(1-phenyl-3-trifluoromethyl)pyrazolyl or 5-(1-(4-chloro-2-pyridinyl)-3-trifluoromethyl)pyrazolyl, then R_5 cannot be:

 $-C(O)-OR_9$, wherein R_9 is $-CH_2-Ar_3$, and the Ar_3 cyclic group is phenyl;

and when R_{11} is Ar_4 , wherein the Ar_4 cyclic group is 5-(1-(2-pyridyl)-3-trifluoromethyl)pyrazolyl), then R_5 cannot be:

- $-C(O)-R_{10}$, wherein R_{10} is $-Ar_3$ and the Ar_3 cyclic group is 4-(dimethylaminomethyl)phenyl, or
- $-C(O)-OR_9$, wherein R_9 is $-CH_2-Ar_3$, and the Ar_3 cyclic group is phenyl, unsubstituted by $-Q_1$; and when

 Y_2 is O, R_3 is $-C(O)-CH_2-T_1-R_{11}$, T_1 is O, and R_{11} is $-C(O)-Ar_4$, wherein the Ar_4 cyclic group is 2,5-dichlorophenyl, then R_5 cannot be:

-C(O)- R_{10} , wherein R_{10} is -Ar₃ and the Ar₃ cyclic group is 4-(dimethylaminomethyl)phenyl, 4-(N-morpholinomethyl)phenyl, 4-(N-

methylpiperazino) methyl) phenyl, 4-(N-(2-

- methyl)imidazolylmethyl)phenyl, 5-benzimidazolyl, 5-benztriazolyl, N-carboethoxy-5-benztriazolyl, N-carboethoxy-5-benzimidazolyl, or
 - $-C(O)-OR_9$, wherein R_9 is $-CH_2-Ar_3$, and the Ar_3 cyclic group is phenyl, unsubstituted by $-Q_1$,; and when
- Y₂ is H₂, R₃ is $-C(O)-CH_2-T_1-R_{11}$, T₁ is O, and R₁₁ is $-C(O)-Ar_4$, wherein the Ar₄ cyclic group is 2,5-dichlorophenyl, then R₅ cannot be:
 - $-C(O)-OR_9$, wherein R_9 is $-CH_2-Ar_3$ and the Ar_3 cyclic group is phenyl.

69-78. (canceled)

79. (previously presented) The compound according to claim 68, selected from the group consisting of:

80. (previously presented) A compound represented by the formula:

wherein:

 R_1 is:

(e10)
$$\begin{array}{c} X_2 \\ R_{21} \\ R_5 - N \\ H \end{array}$$
 , or

$$\begin{array}{c} R_8 \\ R_5 - N \\ H \end{array} \begin{array}{c} O \\ R_6 \end{array} \hspace{0.5cm} ;$$

C is a ring chosen from the set consisting of benzo, pyrido, thieno, pyrrolo, furano, thiazolo, isothiazolo, oxazolo, isoxazolo, pyrimido, imidazolo, cyclopentyl, and cyclohexyl; the ring optionally being singly or multiply substituted by -Q1;

10 R₂ is:

5

m is 1 or 2;

each R_5 is independently selected from the group consisting of:

$$-C(0)-R_{10}$$
,

-C(O)O-R9,

```
Application No. 10/058,522
        Supp. Amdt. dated March 4, 2004
                      -C(0) -N(R_{10})(R_{10})
                      -S(0)_2-R_9,
                      -S(0)_2-NH-R_{10},
                      -C(0) - CH_2 - O - R_9,
                      -C(O)C(O)-R<sub>10</sub>,
 5
                      -R<sub>9</sub>,
                      -H,
                      -C(O)C(O)-OR_{10}, and
                      -C(0)C(0)-N(R_9)(R_{10});
               X_5 is CH or N;
10
               Y_2 is H_2 or O;
15
               R_6 is selected from the group consisting of -H and
         -CH<sub>3</sub>;
               \ensuremath{\text{R}_8} is selected from the group consisting of:
                      -C(0)-R_{10},
                      -C(O)O-R9,
                      -C(0)-N(H)-R_{10}
20
                      -s(0)_2-R_9,
                      -S(0)_2-NH-R_{10},
                      -C(0) - CH_2 - OR_{10},
                      -C(0)C(0)-R_{10};
                      -C(0) - CH_2N(R_{10})(R_{10}),
25
                      -C(0) - CH_2C(0) - O - R_9,
                      -C(0) - CH_2C(0) - R_9,
                      -H, and
                      -C(0)-C(0)-OR_{10};
30
               each R<sub>9</sub> is independently selected from the group
```

consisting of $-Ar_3$ and a $-C_{1-6}$ straight or branched

5

10

15

20

25

alkyl group optionally substituted with $-Ar_3$, wherein the $-C_{1-6}$ alkyl group is optionally unsaturated;

each R_{10} is independently selected from the group consisting of -H, -Ar₃, a -C₃₋₆ cycloalkyl group, and a -C₁₋₆ straight or branched alkyl group optionally substituted with -Ar₃, wherein the -C₁₋₆ alkyl group is optionally unsaturated;

 R_{13} is selected from the group consisting of H, Ar_3 , and a $-C_{1-6}$ straight or branched alkyl group optionally substituted with $-Ar_3$, $-CONH_2$, $-OR_5$, -OH, $-OR_9$, or $-CO_2H$;

each R_{51} is independently selected from the group consisting of R_9 , $-C(O)-R_9$, $-C(O)-N(H)-R_9$, or each R_{51} taken together forms a saturated 4-8 member carbocyclic ring or heterocyclic ring containing -O-, -S-, or -NH-;

each R_{21} is independently selected from the group consisting of -H or a $-C_{1-6}$ straight or branched alkyl group;

each Ar₃ is a cyclic group independently selected from the set consisting of an aryl group which contains 6, 10, 12, or 14 carbon atoms and between 1 and 3 rings and an aromatic heterocycle group containing between 5 and 15 ring atoms and between 1 and 3 rings, said heterocyclic group containing at least one heteroatom group selected from -O-, -S-, -SO-, SO₂, =N-, and -NH-, said heterocycle group optionally containing one or more double bonds, said heterocycle group optionally comprising one or more aromatic rings, and said cyclic

group optionally being singly or multiply substituted by $-Q_1$;

each Q_1 is independently selected from the group consisting of $-NH_2$, $-CO_2H$, -Cl, -F, -Br, -I, $-NO_2$, -CN, =O, -OH, -perfluoro C_{1-3} alkyl, R_5 , $-OR_5$, $-NHR_5$, $-OR_9$, $-N(R_9)(R_{10})$, $-R_9$, $-C(O)-R_{10}$, and O / \ CH₂,

10

15

30

5

provided that when $-Ar_3$ is substituted with a Q_1 group which comprises one or more additional $-Ar_3$ groups, said additional $-Ar_3$ groups are not substituted with another $-Ar_3$.

81. (previously presented) The compound according to claim 80, wherein:

m is 1;

C is a ring chosen from the set consisting of benzo, pyrido, or thieno the ring optionally being singly or multiply substituted by halogen, $-NH_2$, $-NH-R_5$, $-NH-R_9$, $-OR_{10}$, or $-R_9$, wherein R_9 is a straight or branched C_{1-4} alkyl group, and R_{10} is H or a straight or branched C_{1-4} alkyl group;

 R_6 is H;

 R_{13} is H or a C_{1-4} straight or branched alkyl group optionally substituted with $-Ar_3$, -OH, $-OR_9$, $-CO_2H$, wherein the R_9 is a C_{1-4} branched or straight chain alkyl group; wherein Ar_3 is morpholinyl or phenyl,

wherein the phenyl is optionally substituted by $-Q_1$;

 R_{21} is -H or -CH₃;

5

10

15

20

25

30

 R_{51} is a C_{1-6} straight or branched alkyl group optionally substituted with -Ar₃, wherein Ar₃ is phenyl, optionally substituted by -Q₁;

each Ar_3 cyclic group is independently selected from the set consisting of phenyl, naphthyl, thienyl, quinolinyl, isoquinolinyl, pyrazolyl, thiazolyl, isoxazolyl, benzotriazolyl, benzimidazolyl, thienothienyl, imidazolyl, thiadiazolyl, benzo[b]thiophenyl, pyridyl, benzofuranyl, and indolyl, and said cyclic group optionally being singly or multiply substituted by $-Q_1$;

each Q_1 is independently selected from the group consisting of -NH $_2$, -Cl, -F, -Br, -OH, -R $_9$, -NH-R $_5$ wherein R $_5$ is -C(O)-R $_{10}$ or -S(O) $_2$ -R $_9$, -OR $_5$ wherein R $_5$ is -C(O)-R $_{10}$, -OR $_9$, -NHR $_9$, and



wherein each R_9 and R_{10} are independently a $-C_{1-6}$ straight or branched alkyl group optionally substituted with $-Ar_3$ wherein Ar_3 is phenyl;

provided that when $-\mathrm{Ar}_3$ is substituted with a Q_1 group which comprises one or more additional $-\mathrm{Ar}_3$ groups, said additional $-\mathrm{Ar}_3$ groups are not substituted with another $-\mathrm{Ar}_3$.

5

15

82. (previously presented) The compound according to claim 81, wherein R_1 is (w2).

83. (previously presented) The compound according to claim 82, selected from the group consisting of:

84-87.

88. (previously presented) The compound according to claim 80 wherein R_5 is $-C(O)-R_{10}$ or $-C(O)-C(O)-R_{10}$.

(canceled)

89. (previously presented) The compound according to claim 88, wherein $\ensuremath{\text{R}}_{10}$ is $\ensuremath{\text{Ar}}_3.$

90. (previously presented) The compound according to claim 89, wherein:

 $\rm R_{5}$ is -C(O)-R_{10} and R_{10} is Ar_{3}, wherein the Ar_{3} cyclic group is phenyl optionally being singly or

multiply substituted by:

 $-R_9$, wherein R_9 is a C_{1-4} straight or branched alkyl group;

-F,

-Cl,

5

10

15

 $^{-\rm N\,(H)\,^-R_5},$ wherein $^{-\rm R_5}$ is $^{-\rm H}$ or $^{-\rm C\,(O)\,^-R_{10}},$ wherein $\rm R_{10}$ is a $^{-\rm C}_{1-6}$ straight or branched alkyl group optionally substituted with $^{-\rm Ar}_3,$ wherein $\rm Ar_3$ is phenyl,

 $^{-N\,(R_9)\,(R_{10})}\,,$ wherein $\rm R_9$ and $\rm R_{10}$ are independently a $^{-C_{1-4}}$ straight or branched alkyl group, or

-O-R $_5$, wherein R $_5$ is H or a -C $_{1-4}$ straight or branched alkyl group.

91. (previously presented) The compound according to claim 90, selected from the group consisting of:

5

- 92. (previously presented) The compound according to claim 90, wherein Ar_3 is phenyl being singly or multiply substituted at the 3- or 5-position by -Cl or at the 4-position by -NH-R₅, -N(R₉)(R₁₀), or -O-R₅.
- 93. (previously presented) The compound 10 according to claim 92, selected from the group consisting of:

94. (canceled)

5

95. (previously presented) The compound according to claim 90, wherein Ar_3 is phenyl being singly or multiply substituted at the 3- or 5-position by $-R_9$, wherein R_9 is a C_{1-4} straight or branched alkyl

group;

5

and at the 4-position by $-O-R_5$.

96. (previously presented) The compound according to claim 95, selected from the group consisting of:

$$\begin{array}{c} \text{HO} \\ \text{HO} \\ \text{HO} \\ \text{HO} \\ \text{CH}_3 \end{array}$$
; and

5

10

15

97. (canceled)

98. (previously presented) The compound according to claim 89, wherein:

 R_5 is $-C(O)-R_{10}$, wherein R_{10} is Ar_3 and the Ar_3 cyclic group is selected from the group consisting of is indolyl, benzimidazolyl, thienyl, quinolyl, isoquinolyl and benzo[b]thiophenyl, and said cyclic group optionally being singly or multiply substituted by $-Q_1$.

- 99. (previously presented) The compound according to claim 98, wherein the ${\rm Ar}_3$ cyclic group is isoquinolyl, and said cyclic group optionally being singly or multiply substituted by ${\rm -Q}_1$.
- 100. (previously presented) The compound according to claim 99 selected from the group consisting of:

Page 105 of 135

Page 106 of 135

$$CH_3O$$
 , and H , H

101. (canceled)

5

102. (previously presented) The compound according to claim 89, wherein $\rm R_5$ is -C(O)-R_{10}, wherein $\rm R_{10}$ is Ar_3 and the Ar_3 cyclic group is phenyl, substituted by

5

103. (canceled)

104. (previously presented) A compound represented by the formula:

(VII)
$$R_1$$
 R_3 H

10 wherein:

m is 1 or 2;

 $\ensuremath{\mathtt{R}}_1$ is selected from the group consisting of the following formulae:

15

20

$$(w2) \qquad \begin{array}{c} R_8 \\ N \longrightarrow C \\ O \\ R_5 \longrightarrow N \longrightarrow N \end{array}$$

C is a ring chosen from the set consisting of benzo, pyrido, thieno, pyrrolo, furano, thiazolo, isothiazolo, oxazolo, isoxazolo, pyrimido, imidazolo, cyclopentyl, and cyclohexyl, the ring optionally being singly or multiply substituted by $-Q_1$,;

R₃ is selected from the group consisting of:

```
Application No. 10/058,522
       Supp. Amdt. dated March 4, 2004
                    -CN,
                    -C(O)-H,
                    -C(0) - CH_2 - T_1 - R_{11},
                    -C(0)-CH_2-F,
                    -C=N-O-R_9, and
 5
                    -CO-Ar2;
              each R<sub>5</sub> is independently selected from the group
        consisting of:
                    -C(0)-R_{10},
                    -C(O)O-R9,
10
                    -C(0)-N(R_{10})(R_{10})
                    -S(0)_2-R_9,
                    -S(0)_2-NH-R_{10},
                    -C(0)-CH_2-O-R_9,
                    -C(O)C(O)-R<sub>10</sub>.
15
                    -R<sub>9</sub>,
                    -H,
                    -C(O)C(O)-OR_{10}, and
                    -C(0)C(0)-N(R_9)(R_{10});
20
              each T_1 is independently selected from the group
        consisting of -O-, -S-, -S(0)-, and -S(0)_2-;
              {\rm R}_{\rm 6} is selected from the group consisting of -H and
25
        -CH_3;
              R_8 is selected from the group consisting of:
                    -C(0)-R_{10},
                    -C(O)O-R9,
                    -C(0)-NH-R_{10},
                    -S(0)_2-R_9,
30
                    -S(0)_2-NH-R_{10},
```

```
Application No. 10/058,522

Supp. Amdt. dated March 4, 2004

-C(O)-CH_2-OR_{10},
-C(O)C(O)-R_{10},
-C(O)-CH_2-N(R_{10})(R_{10}),
-C(O)-CH_2C(O)-O-R_9,
-C(O)-CH_2C(O)-R_9,
-H, and
-C(O)-C(O)-OR_{10};
```

each R_9 is independently selected from the group consisting of $-Ar_3$ and a $-C_{1-6}$ straight or branched alkyl group optionally substituted with $-Ar_3$, wherein the $-C_{1-6}$ alkyl group is optionally unsaturated;

each R_{10} is independently selected from the group consisting of -H, -Ar₃, a -C₃₋₆ cycloalkyl group, and a -C₁₋₆ straight or branched alkyl group optionally substituted with -Ar₃, wherein the -C₁₋₆ alkyl group is optionally unsaturated;

each \mathbf{R}_{11} is independently selected from the group consisting of:

```
-Ar<sub>4</sub>,
-(CH<sub>2</sub>)<sub>1-3</sub>-Ar<sub>4</sub>,
-H, and
-C(O)-Ar<sub>4</sub>;
```

10

15

25

 R_{15} is selected from the group consisting of -OH, -OAr₃, -N(H)-OH, and -OC₁₋₆, wherein C₁₋₆ is a straight or branched alkyl group optionally substituted with -Ar₃, -CONH₂, -OR₅, -OH, -OR₉, or -CO₂H;

 ${\rm Ar}_2$ is independently selected from the following group, in which any ring may optionally be singly or

5

10

15

20

25

multiply substituted by $-Q_1$ or phenyl, optionally substituted by Q_1 :

(hh)
$$\stackrel{Y}{\longrightarrow}$$
 , and (ii) ,

wherein each Y is independently selected from the group consisting of O and S;

each Ar_3 is a cyclic group independently selected from the set consisting of an aryl group which contains 6, 10, 12, or 14 carbon atoms and between 1 and 3 rings and an aromatic heterocycle group containing between 5 and 15 ring atoms and between 1 and 3 rings, said heterocyclic group containing at least one heteroatom group selected from -O-, -S-, -SO-, SO_2 , =N-, and -NH-, $-N(R_5)$ -, and $-N(R_9)$ - said heterocycle group optionally containing one or more double bonds, said heterocycle group optionally comprising one or more aromatic rings, and said cyclic group optionally being singly or multiply substituted by $-Q_1$;

each Ar_4 is a cyclic group independently selected from the set consisting of an aryl group which contains 6, 10, 12, or 14 carbon atoms and between 1 and 3 rings, and a heterocycle group containing between 5 and 15 ring atoms and between 1 and 3 rings, said heterocyclic group containing at least one heteroatom group selected from -O-, -S-, -SO-, SO_2 , =N-, -NH-, -N(R_5)-, and -N(R_9)- said heterocycle group optionally

5

15

20

containing one or more double bonds, said heterocycle group optionally comprising one or more aromatic rings, and said cyclic group optionally being singly or multiply substituted by $-Q_1$;

each Q_1 is independently selected from the group consisting of $-NH_2$, $-CO_2H$, -Cl, -F, -Br, -I, $-NO_2$, -CN, =O, -OH, -perfluoro C_{1-3} alkyl, R_5 , $-OR_5$, $-NHR_5$, $-OR_9$, $-N(R_9)(R_{10})$, $-R_9$, $-C(O)-R_{10}$, and O

 $-N(R_9)(R_{10})$, $-R_9$, $-C(O)-R_{10}$, and O /\
10 CH_2

provided that when $-\mathrm{Ar}_3$ is substituted with a Q_1 group which comprises one or more additional $-\mathrm{Ar}_3$ groups, said additional $-\mathrm{Ar}_3$ groups are not substituted with another $-\mathrm{Ar}_3$.

105-111. (canceled)

112. (previously presented) The compound according to claim 104, selected from the group consisting of:

113. (canceled)

114. (previously presented) The compound according to claim 68, wherein:

m is 1;

 T_1 is 0 or S;

 R_{21} is -H or -CH₃;

 Ar_2 is (hh);

10 Y is O;

5

15

each Ar_3 cyclic group is independently selected from the set consisting of phenyl, naphthyl, thienyl, quinolinyl, isoquinolinyl, pyrazolyl, thiazolyl, isoxazolyl, benzotriazolyl, benzimidazolyl, thienothienyl, imidazolyl, thiadiazolyl, benzo[b]thiophenyl, pyridyl, benzofuranyl, and indolyl and said cyclic group being singly or multiply substituted by $-Q_1$;

each Ar₄ cyclic group is independently selected from the set consisting of phenyl, tetrazolyl, pyridinyl, oxazolyl, naphthyl, pyrimidinyl, and thienyl

5

10

15

20

and said cyclic group being singly or multiply substituted by $-Q_1$;

each Q_1 is independently selected from the group consisting of $-NH_2$, -Cl, -F, -Br, -OH, $-R_9$, $-NH-R_5$ wherein R_5 is $-C(O)-R_{10}$ or $-S(O)_2-R_9$, $-OR_5$ wherein R_5 is $-C(O)-R_{10}$, $-OR_9$, $-NHR_9$, and

O /\ CH₂,

wherein each R_9 and R_{10} are independently a $-C_{1-6}$ straight or branched alkyl group optionally substituted with $-Ar_3$ wherein Ar_3 is phenyl;

provided that when $-\mathrm{Ar}_3$ is substituted with a Q_1 group which comprises one or more additional $-\mathrm{Ar}_3$ groups, said additional $-\mathrm{Ar}_3$ groups are not substituted with another $-\mathrm{Ar}_3$.

115-117. (canceled)

- 118. (previously presented) The compound according to claims 104 or 114, wherein R_5 is $-C(0)-R_{10}$ or $-C(0)C(0)-R_{10}$.
- 119. (previously presented) The compound according to claim 118, wherein R_{10} is Ar_3 .
 - 120. (previously presented) The compound according to claim 119, wherein:

 R_5 is -C(O)- R_{10} and R_{10} is Ar_3 , wherein the Ar_3

cyclic group is phenyl optionally being singly or multiply substituted by:

 $-R_9$, wherein R_9 is a C_{1-4} straight or branched alkyl group;

-F,

5

10

15

-C1,

 $-N(H)-R_5$, wherein $-R_5$ is -H or $-C(O)-R_{10}$, wherein R_{10} is a $-C_{1-6}$ straight or branched alkyl group optionally substituted with $-Ar_3$, wherein Ar_3 is phenyl,

 $-{\rm N\,(R_9)\,(R_{10})}\,,$ wherein ${\rm R_9}$ and ${\rm R_{10}}$ are independently a $-{\rm C_{1-4}}$ straight or branched alkyl group, or

 $-\text{O-R}_5$, wherein R_5 is H or a $-\text{C}_{1-4}$ straight or branched alkyl group.

121. (previously presented) The compound according to claim 120, selected from the group consisting of:

Page 117 of 135

913
$$H_3C-N$$
 H_3C-N H_3C-N

5

122. (previously presented) The compound according to claim 120, wherein Ar_3 is phenyl being singly or multiply substituted at the 3- or 5-position by -Cl or at the 4-position by -NH-R₅, -N(R₉)(R₁₀), or -O-R₅.

123. (previously presented) The compound according to claim 122, selected from the group consisting of:

5

124. (previously presented) The compound according to claim 122, selected from the group consisting of:

125. (previously presented) The compound according to claim 120, wherein Ar_3 is phenyl being singly or multiply substituted at the 3- or 5-position by $-R_9$, wherein R_9 is a C_{1-4} straight or branched alkyl group;

and at the 4-position by $-O-R_5$.

5

10

126. (previously presented) The compound according to claim 125, selected from the group consisting of:

$$\begin{array}{c} HO \\ O \\ HO \\ CH_3 \end{array}$$

917
$$H_3C$$
 H_3C H_4 H_5 H_6 H_7 H_8 H_8

127. (previously presented) The compound according to claim 125, wherein the compound is:

5

10

15

128. (previously presented) The compound according to claim 119, wherein:

 $\rm R_5$ is -C(O)-R_{10}, wherein R_{10} is Ar_3 and the Ar_3 cyclic group is selected from the group consisting of is indolyl, benzimidazolyl, thienyl, quinolyl, isoquinolyl and benzo[b]thiophenyl, and said cyclic group optionally being singly or multiply substituted by -Q_1.

129. (previously presented) The compound according to claim 128, selected from the group consisting of:

; and

5

130. (previously presented) The compound according to claim 128, wherein the ${\rm Ar}_3$ cyclic group is isoquinolyl, and said cyclic group optionally being singly or multiply substituted by ${\rm -Q}_1$.

131. (previously presented) The compound according to claim 130, wherein the compound is:

132. (canceled)

5

133. (previously presented) The compound according to claim 119, wherein R_5 is $-C(0)-R_{10}$, wherein R_{10} is Ar_3 and the Ar_3 cyclic group is phenyl, substituted by

5

10

15

134. (previously presented) The compound according to claim 133, wherein the compound is:

135. (previously presented) The compound according to claim 133, wherein the compound is:

136-137. (canceled)

138. (previously presented) A method for treating or preventing a disease selected from an IGIF mediated disease, an IFN- γ mediated disease, an inflammatory disease, an autoimmune disease, an infectious disease, a proliferative disease, a neurodegenerative disease, a necrotic disease,

5

10

15

20

25

osteoarthritis, acute pancreatitis, chronic pancreatitis, asthma, rheumatoid arthritis, inflammatory bowel disease, Crohn's disease, ulcerative collitis, cerebral ischemia, myocardial ischemia, adult respiratory distress syndrome, infectious hepatitis, sepsis, septic shock, Shigellosis, glomerulonephritis, systemic lupus erythematosus, scleroderma, chronic thyroiditis, Graves' disease, autoimmune qastritis, insulin-dependent diabetes mellitus (Type I), juvenile diabetes, autoimmune hemolytic anemia, autoimmune neutropenia, thrombocytopenia, myasthenia gravis, multiple sclerosis, psoriasis, lichenplanus, graft vs. host disease, acute dermatomyositis, eczema, primary cirrhosis, hepatitis, uveitis, Behcet's disease, acute dermatomyositis, atopic skin disease, pure red cell aplasia, aplastic anemia, amyotrophic lateral sclerosis and nephrotic syndrome comprising the step of administering to said patient a pharmaceutical composition according to claim 42.

139. (previously presented) The method according to claim 138, wherein the disease is selected from an inflammatory disease; an autoimmune disease, an infectious disease, rheumatoid arthritis, ulcerative collitis, Crohn's disease, hepatitis, adult respiratory distress syndrome, glomerulonephritis, insulin-dependent diabetes mellitus (Type I), juvenile diabetes, psoriasis, graft vs. host disease, and hepatitis.

140-153. (canceled)

5

10

15

treating inflammation, comprising contacting a cell population with an inhibiting effective amount of a reagent that suppresses the protease activity of at least one member of the interleukin-lbeta-converting enzyme (ICE)/CED-3 family, thereby preventing or treating inflammation, wherein said inflammation is due to an inflammatory disease, and wherein said inflammatory disease is selected from the group consisting of arthritis, cholangitis, colitis, encephalitis, endocerolitis, hepatitis, pancreatitis, and reperfusion injury.

155. (New) The method of claim 135, wherein said inflammation is chronic inflammation.

156. (New) The method of claim 135, wherein said inflammation is acute inflammation.

- 157. (New) The method of claim 135, wherein the reagent suppresses the protease activity in an irreversible manner.
- 158. (New) The method of claim 135, wherein the reagent suppresses the protease activity in a reversible manner.
 - 159. (New) The method of claim 135, wherein the reagent is a compound of formula 1:

$$R^2$$
 CO_2R^3
 R^1
 R^2
 CO_2R^3

FORMULA 1

wherein:

5

10

15

20

25

n is 1 or 2;

 R^1 is alkyl, cycloalkyl, (cycloalkyl)alkyl, phenyl, (substituted)phenyl, phenylalkyl, (substituted)phenylalkyl, heteroaryl, (heteroaryl)alkyl or $(CH_2)_mCO_2R^4$, wherein m=1-4, and R^4 is as defined below:

 R^2 is a hydrogen atom, chloro, alkyl, cycloalkyl, (cycloalkyl)alkyl, phenyl, (substituted)phenyl, phenylalkyl, (substituted)phenylalkyl, heteroaryl, (heteroaryl)alkyl or $(CH_2)_pCO_2R_5$, wherein p=0-4, and R^5 is as defined below;

R³ is a hydrogen atom, alkyl, cycloalkyl,
(cycloalkyl)alkyl, phenylalkyl, or
(substituted)phenylalkyl;

R⁴ is a hydrogen atom, alkyl, cycloalkyl, (cycloalkyl)alkyl, phenylalkyl, or (substituted)phenylalkyl;

R⁵ is a hydrogen atom, alkyl, cycloalkyl,
(cycloalkyl)alkyl, phenylalkyl, or
(substituted)phenylalkyl;

A is a natural and unnatural amino acid;

B is a hydrogen atom, a deuterium atom, alkyl, cycloalkyl, (cycloalkyl)alkyl, phenyl,

5

10

15

20

25

(substituted) phenyl, phenylalkyl, (substituted) phenylalkyl, heteroaryl, (heteroaryl) alkyl, halomethyl, CH_2ZR^6 , $CH_2OCO(aryl)$, $CH_2OCO(heteroaryl)$; or $CH_2OPO(R_7)R_8$; where Z is an oxygen or a sulfur atom;

R⁶ is phenyl, substituted phenyl, phenylalkyl, substituted phenylalkyl, heteroaryl, or (heteroaryl)alkyl; and

R⁷ and R⁸ are independently selected from a group consisting of alkyl, cycloalkyl, phenyl, substituted phenyl, phenylalkyl, (substituted phenyl) alkyl, and (cycloalkyl) alkyl; and

X and Y are independently selected from the group consisting of a hydrogen atom, halo, trihalomethyl, amino, protected amino, an amino salt, mono-substituted amino, di-substituted amino, carboxy, protected carboxy, a carboxylate salt, hydroxy, protected hydroxy, a salt of a hydroxy group, lower alkoxy, lower alkylthio, alkyl, substituted alkyl, cycloalkyl, substituted cycloalkyl, (cycloalkyl)alkyl, substituted (cycloalkyl)alkyl, phenyl, substituted phenyl, phenylalkyl, and (substituted phenyl)alkyl; or a pharmaceutically acceptable salt thereof.

160. (New) The method of claim 135, wherein the reagent is a compound of formula 3:

$$\begin{array}{c|c} A & N \\ N \\ N \\ O \\ O \\ O \\ CO_2R^1 \end{array}$$

FORMULA 3

wherein:

5

n is 1 or 2;

m is 1 or 2;

A is R^2CO- , $R^3-O-CO-$, or R^4SO_2- , a group of the formula:

$$R^{5}CONH$$
 R^{8}
 $R^{6}OCONH$
 $R^{7}SO_{2}NH$
 R^{8}
 R^{8}
 R^{8}
 R^{8}
 R^{8}
 R^{8}
 $R^{7}SO_{2}NH$
 R^{8}
 $R^{$

Page 132 of 135

Supp. Amdt. dated March 4, 2004 further wherein: R¹ is a hydrogen atom, alkyl or phenylalkyl; R² is alkyl, cycloalkyl, (cycloalkyl)alkyl, phenyl, phenylalkyl, substituted phenyl, (substituted 5 phenyl)alkyl, heteroaryl, or (heteroaryl)alkyl; R3 is alkyl, cycloalkyl, (cycloalkyl)alkyl, phenylalkyl, or (substituted phenyl)alkyl; R4 is alkyl, cycloalkyl, (cycloalkyl)alkyl, phenyl, phenylalkyl, substituted phenyl, (substituted phenyl)alkyl, heteroaryl, or (heteroaryl)alkyl; 10 R⁵ is alkyl, cycloalkyl, (cycloalkyl)alkyl, phenyl, phenylalkyl, substituted phenyl, (substituted phenyl)alkyl, heteroaryl, or (heteroaryl)alkyl; R6 is alkyl, cycloalkyl, (cycloalkyl)alkyl, phenylalkyl, or (substituted phenyl)alkyl; 15 R7 is alkyl, cycloalkyl, (cycloalkyl)alkyl, phenyl, phenylalkyl, substituted phenyl, (substituted phenyl)alkyl, heteroaryl, or (heteroaryl)alkyl; R8 is an amino acid side chain chosen from the group consisting of natural and unnatural amino acids; 20 B is a hydrogen atom, a deuterium atom, alkyl, cycloalkyl, (cycloalkyl)alkyl, phenyl, phenylalkyl, substituted phenyl, (substituted phenyl)alkyl, heteroaryl, (heteroaryl)alkyl, or halomethyl;

Application No. 10/058,522

a group of the formula:

25

Application No. 10/058,522 Supp. Amdt. dated March 4, 2004 -CH₂XR⁹; wherein R9 is phenyl, substituted phenyl, phenylalkyl, (substituted phenyl)alkyl, heteroaryl, or (heteroaryl)alkyl; and X is an oxygen or a sulfur atom; a group of the formula: 5 -CH2-O-CO-(ARYL); a group of the formula: -CH₂-O-CO-(HETEROARYL); a group of the formula: $-CH_2-O-PO(R^{10})R^{11}$ wherein R^{10} and R^{11} are 10 independently selected from a group consisting of alkyl, cycloalkyl, phenyl, substituted phenyl, phenylalkyl and (substituted phenyl) alkyl; and the pharmaceutically-acceptable salts thereof.

15

Page 134 of 135